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I23 and ((dna or rna) same array)	6

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123 and ((dna or rna) same array)

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Entry 1 of 6

File: USPT

Nov 16, 1999

US-PAT-NO: 5986083

DOCUMENT-IDENTIFIER: US 5986083 A

TITLE: Synthetic oligomers having phosphonate internucleosidyl linkages of undefined chirality mixed with non-phosphonate internucleosidyl linkages

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#) 2. Document ID: US 5985558 A

Entry 2 of 6

File: USPT

Nov 16, 1999

US-PAT-NO: 5985558

DOCUMENT-IDENTIFIER: US 5985558 A

TITLE: Antisense oligonucleotide compositions and methods for the inhibition of c-Jun and c-Fos

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#) 3. Document ID: US 5948680 A

Entry 3 of 6

File: USPT

Sep 7, 1999

US-PAT-NO: 5948680

DOCUMENT-IDENTIFIER: US 5948680 A

TITLE: Antisense inhibition of Elk-1 expression

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#) 4. Document ID: US 5877309 A

Entry 4 of 6

File: USPT

Mar 2, 1999

US-PAT-NO: 5877309

DOCUMENT-IDENTIFIER: US 5877309 A

TITLE: Antisense oligonucleotides against JNK

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [KMC](#) [Image](#) 5. Document ID: US 5854410 A

Entry 5 of 6

File: USPT

Dec 29, 1998

US-PAT-NO: 5854410

DOCUMENT-IDENTIFIER: US 5854410 A

TITLE: Oligonucleoside cleavage compounds and therapies

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
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 6. Document ID: US 5658734 A

Entry 6 of 6

File: USPT

Aug 19, 1997

US-PAT-NO: 5658734

DOCUMENT-IDENTIFIER: US 5658734 A

TITLE: Process for synthesizing chemical compounds

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
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Date	Reference	Claims	KWIC		

Document Number 6

Entry 6 of 6

File: USPT

Aug 19, 1997

DOCUMENT-IDENTIFIER: US 5658734 A

TITLE: Process for synthesizing chemical compounds

ABPL:

The present invention relates to a process for synthesizing on a single substrate a plurality of chemical compounds having diverse structures. The process involves the use of a bilayer photoresist to build up selected regions of the array in a step wise fashion.

BSPR:

Synthesis of a plurality of diverse chemical compounds on a single substrate is known in the art. For example Fodor et al., U.S. Pat. No. 5,445,934 (incorporated herein by reference for all purposes) discloses forming an array by the steps of (i) disposing on a substrate a layer of linker molecules having photoremovable protecting groups; (ii) imagewise exposing the layer to radiation to activate selected regions; (iii) attaching a monomer with photoremovable protecting group to the activated regions and repeating the steps of activation and attachment until a plurality of polymer of the desired length and sequence are synthesized. The method of Fodor et al. has been used to form dense arrays of biological molecules of, for example, oligonucleotides, and is considered pioneering in the industry. The arrays formed according to the methods disclosed in Fodor et al. may be used, for example, in drug discovery, oligonucleotide sequencing, oligonucleotide sequence checking, and other applications.

BSPR:

While Fodor's above technique has met with substantial success, it would be desirable to provide additional and improved techniques for forming arrays of biological materials.

BSPR:

The present invention relates to a process for synthesizing an array comprising a plurality of chemical compounds having diverse structures such as a diverse monomer sequences on a substrate. The first step involves coating a layer of protective polymer onto a layer of foundational molecules which are immobilized on a substrate. The foundational molecules have a labile protecting group on a chemically reactive site. A layer of polymeric, radiation-sensitive photoresist is coated onto the layer of protective polymer. The photoresist layer is exposed to radiation and then developed using one or more solvents to imagewise uncover selected regions of the layer of foundational molecules. The uncovered portions of the layer of foundational molecules are treated to remove the protecting group and activate the molecules. Preferably, the remaining portion of photoresist and protective polymer layers are then stripped off. The last step involves bonding a chemical molecule preferably having a labile protecting group onto an uncovered reactive site of the

foundational molecules. The process steps may then be repeated uncovering other regions of the substrate and reacting the activated layer with other chemical molecules to form the array. The process is conveniently used to make polypeptides and oligo/polynucleotides preferably comprising a few monomers up to about 50 monomers.

BSPR:

As used herein, these terms will have the following meaning: "Oligonucleotide" is a nucleic acid sequence composed of two or more nucleotides. An oligonucleotide can be derived from natural sources but is often synthesized chemically. It is of any size. An "oligonucleotide analogue" refers to a polymer with two or more monomeric subunits, wherein the subunits have some structural features in common with a naturally occurring oligonucleotide which allow it to hybridize with a naturally occurring oligonucleotide in solution. For instance, structural groups are optimally added to the ribose or base of a nucleoside for incorporation into an oligonucleotide, such as a methyl or allyl group at the 2-O position on the ribose, or a fluoro group which substitutes for the 2'-O group, or a bromo group on the ribonucleoside base. The phosphodiester linkage, or "sugar-phosphate backbone" of the oligonucleotide analogue can also be substituted or modified, for instance with methyl phosphates or O-methyl phosphates. Another example of an oligonucleotide analogue for purposes of this disclosure includes "peptide nucleic acids" in which a polyamide backbone is attached to oligonucleotide bases, or modified oligonucleotide bases. Oligonucleotide analogues optionally comprise a mixture of naturally occurring nucleotides and nucleotide analogues.

BSPR:

In the next step of the process, the resist layer is imagewise exposed to radiation, suitably electromagnetic radiation such as ultraviolet, preferably at a wavelength of about 200-550 nm. The preferred radiation source is mercury or mercury-xenon lamp. Preferably, for large-scale manufacturing, the imaging dose is less than 200 mJ/cm.² to enhance throughput of the arrays.

BSPR:

After completion of the synthesis of the desired number of chemical molecules on the array, the protecting groups on the molecules are preferably removed.

BSPR:

The process of the present invention also relates screening biochemical polymers e.g. oligonucleotides for determination of binding affinity using the arrays made by the process of the present invention. For example, fluorescent labeled unknown biochemical polymers or oligomers can be structurally identified by their binding affinities on the array using art known techniques. In such screening unlabeled or labeled receptor such as an oligonucleotide or any one of a variety of other receptors. In one preferred embodiment the polymers are exposed to a first, unlabeled receptor of interest and, thereafter exposed to a labeled receptor-specific recognition element, which is, for example, an antibody. This process will provide signal amplification in the detection stage.

DEPR:

Glass substrates bearing 5'-dimethoxytrityl (DMT) protected phosphoramidite-activated nucleotide foundation molecules were overcoated with a 0.5 .mu.m thick layer of Ciba-Geigy XU218, a commercial polyimide, by spin coating from a 7 weight percent solution in anisole. The substrates were contact baked on a hotplate at 100 degree C. for 60 seconds to remove solvent from the film. The

substrate was then spin coated with a nominal 1 .mu.m film of photoresist and baked for 60 seconds at 100.degree. C. The photoresist composition was comprised of a solution of 16.2 grams of epoxy resin, 1.0 gram triphenylsulfonium hexafluoroantimonate, and 1.0 gram 9-anthracenemethanol in 83.8 grams of cyclohexanone. The bilayer coated wafer was exposed through a mask on a contact aligner with a dose of 54 mJ/cm.sup.2 with a 365 nm bandpass filter in place. The exposed wafer was baked at 100.degree. C. for 60 seconds, quenched on a cold plate, then spray developed on a photoresist spinner with cyclohexanone for 15 seconds at 1500 rpm. The polyimide barrier layer was wet etched on a photoresist spinner by first puddling anisole for 7 seconds, then spinning off the anisole at 1500 rpm and quenching by rinsing with cyclohexanone. The patterned substrates were treated with a 5% solution of dichloroacetic acid in cyclohexanone (v/v) for 10 minutes to remove the DMT from the nucleotide selectively in the exposed regions of the substrate and form reactive hydroxyl groups. No detectable degradation in the bilayer pattern fidelity was observable by visual inspection. The resist was stripped by soaking the plate in methylene chloride for 3 minutes and rinsing with methylene chloride. The substrate was then derivatized with a Fluoreprime(.TM.) fluorescein phosphoramidite and tetrazole in acetonitrile, using an Applied Biosystems Inc (ABI) DNA synthesizer. This step functionalizes the free hydroxyl reactive groups with a fluorescent moiety in order to determine the fidelity of the patterning process. After treatment of the Fluoreprimed samples with an ethylene diamine/ethanol mixture, the fluorescent array scanner to determine the regions where the fluorescent phosphoramidite moiety coupled to the reactive hydroxyl group. A pattern resolution of 8 micron lines and spaces was achieved.

CLPV:

(a) exposing an array to biochemical polymers, the array comprising a plurality of biochemical compounds having diverse structure bonded to a substrate and made by the process of;

CLPV:

(b) detecting on the array the locations of binding of the biochemical polymer to the biochemical compounds.

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Entry 1 of 6

File: USPT

Nov 16, 1999

US-PAT-NO: 5986083

DOCUMENT-IDENTIFIER: US 5986083 A

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Nov 16, 1999

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Sep 7, 1999

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File: USPT

Dec 29, 1998

US-PAT-NO: 5854410

DOCUMENT-IDENTIFIER: US 5854410 A

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Terms	Documents
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Terms	Documents
((acid or acidic or (low pH))near3 (stable or stability))	12701

Database: US Patents Full-Text Database ▾Refine Search: ((acid or acidic or (low pH))near3
(stable or stability)) ▾**Search History**

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USPT	11 and ((acid or acidic or (low pH))near3 (stable or stability))	0	<u>L4</u>
USPT	11 and (acid near3 (stable or stability))	0	<u>L3</u>
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USPT	05811538	1	<u>L1</u>